

522-1771

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE THE APPLICATION OF )  
Cauwenberghs et al ) Examiner:  
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 SERIAL NO.: )  
 )  
 FILED: ) Group Art Unit:  
 )  
 FOR: DETECTION OF )  
 VON-WILLEBRANDFACTOR )  
 (vWF) ACTIVITY )

AMENDMENT ACCOMPANYING APPLICATION

Honorable Director of Patents  
and Trademarks  
Washington, D.C. 20231

Dear Sir:

The present application is the national filing of International Application No. PCT/EP00/06345. Before calculation of the national filing fee for the United States, it is requested that the application be amended as follows:

In the claims:

Cancel claims 1 – 30 without prejudice and substitute new claims 31 – 47 as follows:

31. A method for the discrimination between von Willebrand disease (vWD) type 1 and type 2 comprising the steps of:  
a) detecting vWF activity in a test sample according to the method for detecting von-Willebrand factor (vWF) activity comprising assaying a sample in the presence of a soluble form or portion of glycoprotein Ib (a) (GPIb (a)) and ristocetin, or a functionally equivalent substance.  
b) determining the amount of vWF-antigen in said test sample

c) determining the ratio between vWF-activity and vWF-antigen for said test sample; and d) comparing the under (c) obtained ratio to the range of ratios established as normal range.

32. The method of claim 31, wherein said detection of von-Willebrand factor (vWF) activity is carried out by detecting the formation of a complex of vWF and GPIb (a) and/or a formed complex of vWF and GPIb (a).

33. The method of claim 31, wherein said GPIb (a) is bound to a solid support.

34. The method of claim 31, wherein said GPIb (a) is bound to said solid support by a specifically reacting anti-GPIb (a) antibody.

35. The method of claim 31, wherein detection of von-Willebrand factor (vWF) activity is carried out by detecting the formation of a complex of vWF and GPIb (a) and/or a formed complex of vWF and GPIb and wherein said complex is bound to a solid support.

36. The method of claim 31, wherein detection of von-Willebrand factor (vWF) activity is carried out by detecting the formation of a complex of vWF and GPIb (a) and/or a formed complex of vWF and GPIb and wherein said complex is bound to a solid support by a specifically reacting anti-GPIb (a) antibody, by a specifically reacting anti-vWF antibody, by a specifically reacting anti-Factor VIII antibody and/or by collagen.

37. The method of claim 31, wherein said detection is carried out by a specifically reacting anti-vWF antibody, by a specifically reacting anti Factor VIII antibody, by a specifically reacting anti-GPIb (a) antibody, by collagen and/or mixtures thereof.

38. The method of claim 31 wherein said detection is carried out by an heterogeneous or by an homogeneous assay.

39. The method of claim 31, wherein said detection is carried out by an heterogenous assay selected from the group of linked immuno sorbent assay (ELISA), a radioimmunoassay (RIA), an immuno radio metric assay (IRMA), a fluorescent immunoassay (FIA), a chemiluminescent immuno assay (CLIA) or an electro chemiluminescent immuno assay (ECL).

40. The method of claim 31, wherein said detection is carried out by an homogenous agglutination assay.

41. The method of claim 31 wherein the sample is selected from the group of a diluted or undiluted blood or plasma sample.

42. Use of a soluble form or portion of glycoprotein Ib (a) (GPIb (a)) for the discrimination between von Willebrand disease (vWD) type 1 and type 2 carrying out the steps of:

- a) detecting vWF activity in a test sample according to the method for detecting von-Willebrand factor (vWF) activity comprising assaying a sample in the presence of a soluble form or portion of glycoprotein Ib (a) (GPIb (a)) and ristocetin, or a functionally equivalent substance.
- b) determining the amount of vWF-antigen in said test sample;

43. Use of ristocetin or a functional equivalent substance of istocetin for the discrimination between von Willebrand disease (vWD) type 1 and type 2 of for carrying a) detecting vWF activity in a test sample according to the method for detecting von-Willebrand factor (vWF) activity comprising assaying a sample in the presence of a soluble form or portion of glycoprotein Ib (a) (GPIb (a)) and ristocetin, or a functionally equivalent substance. b) determining the amount of vWF-antigen in said test sample;